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(54) **CATALYTICALLY INACTIVE TRUNCATED GUIDE RNA COMPOSITIONS AND RELATED METHODS FOR SUPPRESSION OF CRISPR/CAS OFF-TARGET EDITING**

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(57) **ABSTRACT**

The disclosure provides compositions and methods for suppressing off-target editing guide RNA-nuclease complexes. The disclosed strategies incorporate use of catalytically inactive truncated guide RNA/nuclease complexes to shield off-target editing. In some embodiments, the disclosure provides a method of inhibiting off-target cleavage of DNA by a first guide RNA-endonuclease complex by contacting the DNA with a second guide RNA-endonuclease complex that comprises a second guide RNA corresponding to the off-target site but with a recognition sequence of 16 or fewer nucleotides. In another aspect, the disclosure provides a method for preventing cleavage of DNA after editing and subsequent homology-directed repair (HDR) by contacting the repaired DNA with a guide RNA-endonuclease complex that comprises a guide RNA with a guide RNA corresponding to the repaired sequence but with a recognition sequence of 16 or fewer nucleotides. Additional methods, compositions, and kits are also provided.

Specification includes a Sequence Listing.